Complete Summary

GUIDELINE TITLE

Practice guidelines for the treatment of Lyme disease.

BIBLIOGRAPHIC SOURCE(S)

Wormser GP, Nadelman RB, Dattwyler RJ, Dennis DT, Shapiro ED, Steere AC, Rush TJ, Rahn DW, Coyle PK, Persing DH, Fish D, Luft BJ. Practice guidelines for the treatment of Lyme disease. Clin Infect Dis 2000 Jul;31(Suppl 1):1-14. [99 references]

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Lyme disease

GUIDELINE CATEGORY

Management
Prevention
Treatment

CLINICAL SPECIALTY

Family Practice
Infectious Diseases
Internal Medicine
Neurology
Rheumatology

INTENDED USERS

Allied Health Personnel
Physicians

GUIDELINE OBJECTIVE(S)

To provide clinicians and other health care practitioners with recommendations for the management of patients diagnosed with Lyme disease, or patients bitten by an Ixodes tick in North America

TARGET POPULATION

Patients with Lyme disease or patients bitten by an Ixodes tick in North America

INTERVENTIONS AND PRACTICES CONSIDERED

Prevention

1. Avoid tick-infested areas
2. Use of protective clothing
3. Inspection of entire body to locate and remove ticks
4. Tick and insect repellent
5. Outer-surface protein A (OspA) vaccine

Treatment-Oral

1. Amoxicillin
2. Doxycycline
3. Cefuroxime axetil
4. Azithromycin
5. Erythromycin
6. Clarithromycin

Treatment-Parenteral

1. Ceftriaxone
2. Cefotaxime
3. Penicillin G

MAJOR OUTCOMES CONSIDERED

- Prevention of Lyme disease
- Prevention of other Ixodes-borne illnesses, including babesiosis and human granulocytic ehrlichiosis
- Resolution of symptoms and signs of early Lyme disease and prevention of late complications
- Effective treatment of late complications of Lyme disease while minimizing the adverse effects of antibiotic therapy
- Risks and consequences of developing Lyme disease
- Cost and adverse effects of antimicrobial therapy
- Quality of life

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Grades reflecting the quality of evidence on which recommendations are based:

I. Evidence from at least one properly randomized, controlled trial
II. Evidence from at least one well-designed clinical trial without randomization, from cohort or case-controlled analytic studies (preferably from more than one center), from multiple time-series studies, or from dramatic results of uncontrolled experiments
III. Evidence from opinions of respected authorities based on clinical experience, descriptive studies, or reports of expert committees

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not applicable

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Strength of recommendation:

A. Good evidence to support a recommendation for use

B. Moderate evidence to support a recommendation for use
C. Poor evidence to support a recommendation
D. Moderate evidence to support a recommendation against use
E. Good evidence to support a recommendation against use

COST ANALYSIS

Tick Bites and Prophylaxis

One cost-effectiveness analysis concluded that a 2-week course of doxycycline is indicated when the probability of infection with B. burgdorferi after a tick bite is >.036 and should be considered when the theoretical probability ranges from .01 to .035.

Late Lyme Disease

In a cost-effectiveness analysis, intravenous (IV) therapy was found to be no more cost-effective than oral therapy for patients with Lyme arthritis; iv therapy was more likely to result in serious complications and was substantially more expensive. Therefore, the authors concluded that oral antibiotics are to be preferred in the initial treatment of Lyme arthritis in the absence of concomitant neurological involvement.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Excerpted by the National Guideline Clearinghouse (NGC)

Each recommendation includes a ranking for the strength and the quality of evidence supporting it. Definitions of the levels of evidence (I-III) and grades of recommendation (A-E) are repeated at the end of the Major Recommendations field.

Note: See Tables 3 and 4 of the original guideline document for recommended antimicrobial regimens for the treatment of Lyme disease in adults and children.

Tick bites and prophylaxis

Primary Management Options

The best currently available method for preventing infection with Borrelia burgdorferi and other Ixodes-transmitted infections is to avoid vector tick exposure. If exposure to Ixodes scapularis or Ixodes pacificus ticks is unavoidable, measures recommended to reduce the risk of infection include using both protective clothing and tick repellents, checking the entire body for ticks daily, and promptly removing attached ticks before transmission of Borrelia burgdorferi can occur (A-III).

Routine use of either antimicrobial prophylaxis (E-I) or serological tests (D-III) after a tick bite is not recommended. Some experts recommend antibiotic therapy for patients bitten by Ixodes scapularis ticks that are estimated to have been attached for greater than 48 hours (on the basis of the degree of engorgement of the tick with blood), in conjunction with epidemiological information regarding the prevalence of tick-transmitted diseases (C-III). However, accurate determinations of tick species and degree of engorgement are not routinely possible, and data are insufficient to demonstrate efficacy of antimicrobials in this setting.

Persons who remove attached ticks should be monitored closely for signs and symptoms of tick-borne diseases for up to 30 days and specifically for the occurrence of a skin lesion at the site of the tick bite (which may suggest Lyme disease) or a temperature >38ÂºC (which may suggest human granulocytic ehrlichiosis or babesiosis). Persons who develop a skin lesion or other illness within 1 month after removing an attached tick should promptly seek medical attention for assessment of the possibility of having acquired a tick-borne disease (A-II). Health care practitioners, particularly those in areas where Lyme disease is endemic, should become familiar with the clinical manifestations of and recommended practices for testing and therapy for Lyme disease, as well as for human granulocytic ehrlichiosis (HGE) and babesiosis (A-III).

Testing of ticks for tick-borne infectious organisms is not recommended, except in research studies (D-III). Prior vaccination with the recently licensed recombinant outer-surface protein A (OspA) vaccine preparation reduces the risk of developing Lyme disease associated with tick bites but should not alter the above recommendations (A-I).

Early Lyme disease

Primary Management Options

Administration of doxycycline (100 mg twice daily) or amoxicillin (500 mg 3 times daily) for 14–21 days is recommended for treatment of early localized or early disseminated Lyme disease associated with erythema migrans, in the absence of neurological involvement or third-degree atrioventricular heart block (see Tables 3 and 4 of the original guideline document) (A-I). In prospective studies, these agents have been shown to be effective in treating erythema migrans and associated symptoms.

Doxycycline has the advantage of being efficacious for treatment of human granulocytic ehrlichiosis (HGE), which may occur simultaneously with early Lyme disease. Doxycycline is relatively contraindicated during pregnancy or lactation and for children aged less than 8 years. Because of its higher cost, cefuroxime

axetil, which is as effective as doxycycline in the treatment of erythema migrans (A-I), should be reserved as an alternative agent for those patients who can take neither doxycycline nor amoxicillin. For children, amoxicillin or doxycycline (for those aged greater than or equal to 8 years) is recommended (see Tables 3 and 4 of the original guideline document) (B-II). Cefuroxime axetil is an acceptable alternative agent (B-III).

Administration of macrolide antibiotics is not recommended as first-line therapy for early Lyme disease (E-I). When used, they should be reserved for patients who are intolerant of amoxicillin, doxycycline, and cefuroxime axetil (see Tables 3 and 4 of the original guideline document). Patients treated with macrolides should be closely followed.

Ceftriaxone (2 grams intravenously daily), although effective, is not superior to oral agents and is therefore not recommended as a first-line agent for treatment of Lyme disease in the absence of neurological involvement or third-degree atrioventricular heart block (E-I).

The use of ceftriaxone (2 grams once daily intravenously for 14–28 days) in early Lyme disease is recommended for acute neurological disease manifested by meningitis or radiculopathy (see Tables 3 and 4 of the original guideline document) (B-II). Parenteral therapy penicillin G or cefotaxime may also be a satisfactory alternative (B-II). For adult patients who are intolerant of both penicillin and cephalosporins, doxycycline (200–400 mg/day in 2 divided doses given orally [or intravenously if the patient is unable to take oral medications]) for 14–28 days may be adequate (B-II).

For children, intravenous ceftriaxone (B-II) or cefotaxime (B-III) is recommended; penicillin G given intravenously is an alternative (B-II).

Patients with first- or second-degree atrioventricular heart block associated with early Lyme disease should be treated in the same manner as patients with erythema migrans without carditis (B-III). We recommend that patients with third-degree atrioventricular heart block be treated with parenteral antibiotics such as ceftriaxone in the hospital, although there are no clinical trial data to support this recommendation (B-III). A temporary pacemaker may also be required.

Although antibiotic treatment does not hasten the resolution of seventh-cranial-nerve palsy associated with Borrelia burgdorferi infection, antibiotics should be given to prevent further sequelae (B-II). There was disagreement among panel members on the neurological evaluation of patients with seventh-cranial-nerve palsy. Some members perform a cerebral spinal fluid examination on all patients with seventh-cranial-nerve palsy, whereas others reserve lumbar puncture for patients for whom there is strong clinical suspicion of central nervous system involvement (e.g., severe headache or nuchal rigidity).

Patients whose cerebral spinal fluid examinations yield normal findings may be treated with the same regimens used for patients with erythema migrans (B-III), whereas patients for whom there is clinical and laboratory evidence of central nervous system involvement should be treated with regimens effective against meningitis (see Tables 3 and 4 of the original guideline document) (B-II).

Treatment for pregnant patients can be identical to that for nonpregnant patients with the same disease manifestation, except that tetracyclines should be avoided (B-III).

Late Lyme Disease

Lyme arthritis

Lyme arthritis usually can usually be treated successfully with antimicrobial agents administered orally or intravenously. Administration of doxycycline or amoxicillin, in each instance for 28 days, is recommended for patients without clinically evident neurological disease (B-II). For children, doxycycline (for those aged greater than or equal to 8 years) or amoxicillin (see Tables 3 and 4 of the original guideline document) (B-II). Oral therapy is easier to administer than intravenous antibiotics, is associated with fewer serious complications, and is considerably less expensive. Its disadvantage is that some patients treated with oral agents have subsequently manifested overt neuroborreliosis, which may require intravenous therapy for successful treatment. Further controlled trials are needed to compare oral with intravenous therapy.

Neurological evaluation, including lumbar puncture, should be done for patients for whom there is a strong clinical suspicion of neurological involvement. Patients with arthritis and objective evidence of neurological disease should receive intravenous ceftriaxone (A-II). Alternative parenteral agents include intravenous cefotaxime (B-III) and intravenous penicillin G (B-II). The long-acting benzathine preparation of penicillin achieves only low levels in the blood and therefore is not recommended (D-III). For children, ceftriaxone intravenously (B-III) or cefotaxime (B-III) is recommended (see Tables 3 and 4 of the original guideline document); penicillin G administered intravenously is an alternative.

For patients who have persistent or recurrent joint swelling after recommended courses of antibiotic therapy, we recommend repeat treatment with another 4-week course of oral antibiotics or with a 2- to 4-week course of ceftriaxone intravenously (see Tables 3 and 4 of the original guideline document) (B-III). Clinicians should consider waiting several months before initiating repeat treatment with antimicrobial agents, because of the anticipated slow resolution of inflammation after treatment. If patients have persistent arthritis despite 2 courses of oral therapy or one course of intravenous therapy, symptomatic treatment with nonsteroidal anti-inflammatory agents is recommended; intra-articular steroids may also be of benefit (B-III). If persistent synovitis is associated with significant pain or if it limits function, arthroscopic synovectomy can reduce the period of joint inflammation (B-II).

Late neuroborreliosis affecting the central nervous system or peripheral nervous system

For patients with late neurological disease affecting the central nervous system or peripheral nervous system, treatment with ceftriaxone (2 grams once a day intravenous for 2–4 weeks) is recommended (see Tables 3 and 4 of the original guideline document) (B-II). Alternative parenteral therapy may include administration of cefotaxime (B-II) or penicillin G (B-II). Response to treatment

is usually slow and may be incomplete. However, unless relapse is shown by reliable objective measures, repeat treatment is not recommended. For children, treatment with ceftriaxone is recommended (see Tables 3 and 4 of the original guideline document) (B-II). Cefotaxime or penicillin G intravenously are alternatives (B-II).

Chronic Lyme disease or post–Lyme disease syndrome

Following an episode of Lyme disease that is treated appropriately, some persons have a variety of subjective complaints (such as myalgia, arthralgia, or fatigue). Some of these patients have been classified as having "chronic Lyme disease" or "post–Lyme disease syndrome," which are poorly defined entities. These patients appear to be a heterogeneous group. Although European patients rarely have been reported to have residual infection (or perhaps reinfection) with Borrelia burgdorferi, this has yet to be substantiated either in a large series of appropriately treated European patients or in a study of North American patients. Residual subjective symptoms that last weeks or months also may persist after other medical diseases (both infectious and noninfectious). It has also been recognized that the prevalence of fatigue and/or arthralgias in the general population is greater than 10%.

In areas of endemicity, coinfection with Borrelia microti or the Ehrlichia species that causes human granulocytic ehrlichiosis (HGE) may explain persistent symptoms for a small number of these patients. Randomized controlled studies of treatment of patients who remain unwell after standard courses of antibiotic therapy for Lyme disease are in progress. To date, there are no convincing published data showing that repeated or prolonged courses of either oral or intravenous antimicrobial therapy are effective for such patients. The consensus of the Infectious Diseases Society of America (IDSA) expert-panel members is that there is insufficient evidence to regard "chronic Lyme disease" as a separate diagnostic entity.

Definitions of Strength of Recommendation and Quality of Evidence Ratings:

Quality of evidence:

I. Evidence from at least one properly randomized, controlled trial
II. Evidence from at least one well-designed clinical trial without randomization, from cohort or case-control analytic studies (preferably from more than one center), from multiple time-series studies, or from dramatic results of uncontrolled experiments
III. Evidence from opinions of respected authorities based on clinical experience, descriptive studies, or reports of expert committees

Strength of recommendation:

A. Good evidence to support a recommendation for use
B. Moderate evidence to support a recommendation for use
C. Poor evidence to support a recommendation
D. Moderate evidence to support a recommendation against use
E. Good evidence to support a recommendation against use

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Patients with early Lyme disease are treated to resolve their signs and symptoms, but also to prevent late complications, which may require further antibiotics.

POTENTIAL HARMS

Oral therapy is easier to administer than intravenous antibiotics, is associated with fewer serious complications, and is considerably less expensive. Its disadvantage is that some patients treated with oral agents have subsequently manifested overt neuroborreliosis, which may require intravenous therapy for successful treatment.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Staying Healthy

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Wormser GP, Nadelman RB, Dattwyler RJ, Dennis DT, Shapiro ED, Steere AC, Rush TJ, Rahn DW, Coyle PK, Persing DH, Fish D, Luft BJ. Practice guidelines for the treatment of Lyme disease. Clin Infect Dis 2000 Jul;31(Suppl 1):1-14. [99 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2000 Jul

GUIDELINE DEVELOPER(S)

Infectious Diseases Society of America - Medical Specialty Society

SOURCE(S) OF FUNDING

Infectious Diseases Society of America (IDSA)

GUIDELINE COMMITTEE

Infectious Diseases Society of America (IDSA) Practice Guidelines Committee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Authors: Gary P. Wormser, Robert B. Nadelman, Raymond J. Dattwyler, David T. Dennis, Eugene D. Shapiro, Allen C. Steere, Thomas J. Rush, Daniel W. Rahn, Patricia K. Coyle, David H. Persing, Durland Fish, and Benjamin J. Luft.

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

An update is not in progress at this time.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the Infectious Diseases Society of America (IDSA) Web site. Also available in HTML format.

Print copies: Available from the University of Chicago Press; fax: (773) 702-6096.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Kish MA. Guide to development of practice guidelines. Clinical Infectious Diseases 2001;32:851-4.
- Gross PA. Practice guidelines for infectious diseases: Rationale for a work in progress. Clin Infect Dis. 1998 May;26(5):1037-41.
- Gross PA, Barrett TL, Dellinger EP, Krause PJ, Martone WJ, McGowan JE Jr, Sweet RL, Wenzel RP. Purpose of quality standards for infectious diseases. Infectious Diseases Society of America. Clin Infect Dis 1994 Mar;18(3):421.

Electronic copies: Available from the Infectious Diseases Society of American (IDSA) Web site.

Print copies: Available from Infectious Diseases Society of America, 66 Canal Center Plaza, Suite 600, Alexandria, VA 22314.

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on May 1, 2001. The information was verified by the guideline developer as of June 29, 2001.

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Date Modified: 11/15/2004